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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,054	SOARES ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *7,9,11,21,23,25,28 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,10,12,13,18-20,22,24,26,27 and 29-31* is/are rejected.

7)☒ Claim(s) *1,5,10,24,26,27 and 29* is/are objected to.

8)☒ Claim(s) *1-32* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/06;2/27/08;8/3/09;1/5/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: PTO-90C Sequence Compliance Letter; PTO-Notice to Comply with Sequence Disclosure Requirements.

DETAILED ACTION

Status of Application, Amendments and/or Claims

Claims 1-32 are pending in the instant application.

Election/Restrictions

Applicants' election without traverse of Group I, claims 1-13 and 18-32, in the reply filed on 1/21/10 is acknowledged.

Claims 14-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 1/21/10.

Two elections of species were required if Group I was elected:

(1) Applicants' election of SEQ ID NO: 137 as the species of peptide in the reply filed on 1/21/10 is acknowledged.

At pg 1 of the response, Applicants indicate that claims 1-6, 8, 10, 12-13, 18-20, 22, 24, 26, 27 and 29 read on SEQ ID NO: 137. The Examiner agrees, and also considers that claims 30 and 31 read on the elected species; claim 32 does not as it depends from claim 28.

Claims 7, 9, 11, 21, 23, 25, 28 and 32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

(2) Applicants' election of polyethylene glycol (PEG) as the species of polymer in the reply filed on 1/21/10 is acknowledged.

At pg 1 of the response, Applicants indicate that claims 30-32 read on PEG. The Examiner agrees.

Claims 1-6, 8, 10, 12-13, 18-20, 22, 24, 26, 27 and 29-31 are under consideration, as they read upon the elected species.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Specifically, "formula I" in claim 5, and in the specification at ¶ [0087] (as published), is identified as SEQ ID NO: 34, but does not match SEQ ID NO: 34 in the Sequence Listing (filed 6/19/08). Specifically, in SEQ ID NO: 34, residues 2 and 7 are identified as "any amino or not present", but in "formula I", residues 2 and 7 are only identified as "X" and "Y".

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Please see attached PTO-90C and PTO-Notice to Comply.

Specification

The disclosure is objected to because of the following informalities:

(1) The title of the invention ("AMYLIN FAMILY PEPTIDES AND METHODS FOR MAKING AND USING THEM") is not descriptive because (1) there are no claims directed to method for making peptides and (2) the claims to methods for using the peptides are limited to methods of using them for treatment. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: “AMYLIN FAMILY PEPTIDES AND METHODS FOR USING THEM FOR TREATMENT”.

(2) The disclosure is objected to because the Brief Description of Figure 6 on page 35 does not refer to Figure 6C. See 37 CFR § 1.74, which states “When there are drawings, there shall be a brief description of the several views of the drawings and the detailed description of the invention shall refer to the different views by specifying the numbers of the figures and to the different parts by use of reference letters or numerals (preferably the latter)” and MPEP 601.01(g) which states “if the drawings show Figures 1A, 1B, and 1C and the brief description of the drawings refers only to Figure 1, this is an error in the specification which must be corrected.”

(3) The disclosure is also objected to because the Brief Description of Figure 6 refers to each of parts 6A and 6B with the same description without distinguishing them. The description should indicate that Figure 6A shows the results at 1 Week, Figure 6B shows the results at 2 weeks, and Figure 6C shows the results at 3 weeks.

(4) The disclosure is also objected to because the Brief Description of Figure 7 refers to each of parts 7A-E with the same description without distinguishing them. The description should indicate that Figure 7A shows the baseline results, Figure 7B shows the results at 2 weeks, Figure 7C shows the results at 4 weeks, Figure 7D shows the results at 6 weeks, and Figure 7E shows the results at 8 weeks.

(5) The disclosure is also objected to because the Brief Description of Figure 8 refers to each of parts 8A-C with the same description ("the effect of ghrelin by amylin") without distinguishing them. The description should indicate what is different in each of Figures 8A, 8B and 8C.

(6) The disclosure is also objected to because the Brief Description of Figure 9 refers to each of parts 9A and B with the same description ("the effect of on a marker of pancreatic function by an exemplary compound of the invention") without distinguishing them. The description should indicate what that 9A shows a marker that is plasma amylase, and that 9B shows a marker that is plasma lipase.

(7) The disclosure is also objected to because the Brief Description of Figure 11 refers to each of parts 11A and B with the same description ("the gastroprotective effect of amylin") without distinguishing them. The description should indicate what is different in each of Figures 11A and B.

(8) The disclosure of "formula I" at ¶ [0087] of the specification (as published) is objected for the reason set forth above in the section titled "Sequence Compliance".

(9) The table on pages 62-67 of the specification as originally filed was amended on 8/10/06 to indicate the SEQ ID NOs of compounds 1-127. However, compounds 90 and 101 have each been identified as SEQ ID NO: 110 (page 66 of the specification; page 5 of Applicants' 8/10/06 response). It is believed that the compound 101 should be identified as SEQ ID NO: 120.

(10) The tables in the specification are not labeled in numerical order. The first table shown on pages 1-2 is correctly labeled "Table 1". The next table, on page 61, is labeled "Table X"; this should be changed to "Table 2". The next table, on pages 62-67, is unlabeled; this should be changed to "Table 3". The next table, on page 68, is labeled "Table X"; this should be changed to "Table 4".

Appropriate correction is required.

Claim Objections

Claims 1, 5, 10, 24, 26, 27 and 29 are objected to because of the following informalities:

(1) Claim 1 ends with two periods.

(2) Claim 5 is objected for the reason set forth above in the section titled "Sequence Compliance".

(3) Claim 10 contains an extraneous comma on line 4 between "Xaa32" and "(SEQ ID NO: 36). This comma should either be deleted (see claim 9, which is constructed similarly and contains no comma in this location).

(4) Claims 24, 26, 27 and 29 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 24 and 29 depend from claim 23 and claim 28 (respectively), which are withdrawn as not reading on SEQ ID NO: 137 (Applicants indicated that claims 23 and 29 do not read on the elected species in the 1/21/10 response). However, claim 24 recites SEQ ID NO: 137. Thus, claim 24 fails to limit parent claim 23. Claims 26 and 27 depend from claims 24 and 26 (respectively) and also fail to limit parent claim 23.

Appropriate correction is required.

Claim Rejections - 35 USC § 112,2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5, 6, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation “said amylin” in line 1. The antecedent basis for this limitation is unclear. Specifically, claim 2 depends from claim 1, which recites the term "amylin" in line 1, line 2 (two recitations), line 6 and line 7. Each of these recitations of "amylin" can independently be limited to "human amylin". Thus, it is not clear whether dependent claim 2 limits all recitations of amylin in parent claim 1 to "human amylin", or just one or more (and if so, which one(s)). For purposes of prosecution, claim 2 will be interpreted as if any of the recitations of amylin in parent claim 1 can be limited to "human amylin".

Claim 3 recites the limitation “said calcitonin” in line 1. The antecedent basis for this limitation is unclear. Specifically, claim 3 depends from claim 1, which recites the term "calcitonin" in line 2 (two recitations), line 4, line 5, line 7, line 8 (two recitations) and line 9 (two recitations). Each of these recitations of "calcitonin" can independently be limited to "salmon calcitonin". Thus, it is not clear whether dependent claim 3 limits all recitations of calcitonin in parent claim 1 to "salmon calcitonin", or just one or more (and if so, which one(s)). For purposes of prosecution, claim 3 will be interpreted as if any of the recitations of calcitonin in parent claim 1 can be limited to "salmon calcitonin".

Claim 4 recites the limitation “said calcitonin” in line 1. The antecedent basis for this limitation is unclear. Specifically, claim 4 depends from claim 2, which in turn depends from claim 1, which recites the term "calcitonin" in line 2 (two recitations), line 4, line 5, line 7, line 8 (two recitations) and line 9 (two recitations). Thus, claim 4 is indefinite for the same reason as claim 3 described above.

Claim 5 is indefinite because the term "Y" is used with two different meanings in formula I the claim. Specifically, "Y" is used in line 3 as part of the backbone of SEQ ID NO: 34, but is also used as part of the various Xaa descriptors (e.g., Xaa1 (line 7), Xaa5 (line 11) etc). The final three lines of the claim recite "wherein X and Y are capable…"

These usages render unclear which of the usages of "Y" refers to a tyrosine amino acid residue, and/or which are being referred to in the last three lines of the claim.

Claim 6 is rejected for depending from indefinite claim 5.

Claims 18 and 19 are each indefinite for the same reasons as for claim 5.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8, 10, 12, 18-20, 22, 24, 26, 27 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

An amylin family peptide having at least 87% sequence identity to the amino acid sequence of SEQ ID NO: 137, and wherein said peptide reduces food intake when administered to a mouse,

does not reasonably provide enablement for

An amylin family peptide, said peptide comprising: a loop region of amylin, calcitonin, or an analog of amylin or calcitonin, wherein said loop region is at the N-terminal end of said peptide; an α helix region of a) at least a portion of a calcitonin α helix region or an analog thereof or b) a combination of at least a portion of a calcitonin α helix region or an analog thereof and at least a portion of an amylin α helix region or an analog thereof; and a C-terminal tail of amylin, calcitonin, or an analog of amylin or calcitonin; with the proviso that when the loop region is from a calcitonin or a calcitonin analog and the α helix region is from a calcitonin or a calcitonin analog, the last position of the C-terminal tail is not proline, hydroxyproline, homoserine or derivative of homoserine.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a peptide comprising sequences derived from the peptides amylin and/or calcitonin. The specification at pg 1 provides a table (Table 1) summarizing the biological effects of amylin and calcitonin, including an "anorectic effect" (appetite suppression). The specification discloses the naturally occurring sequences of human and rat amylin as SEQ ID NO: 1 and 2 (each peptide 37 amino acids in length), and of salmon and human calcitonin as SEQ ID NO: 3 and 4 (each peptide 32 amino acids in length). The instant specification teaches that amino acids 1-7 of calcitonin are the loop region, amino acids 8-27 are the α helix region, and amino acids 27- or 28-32 are the C-terminal region.

The specification provides the following working examples in support of the claimed invention. Example 1 (pg 59) describes standard methods used for peptide synthesis. Example 2 (pg 59-61) is titled "Receptor Binding Assays" and shows the results of the binding of Compounds 1-9 to the calcitonin receptor. Compounds 1-5, 7 and 9 are elsewhere identified as SEQ ID NO: 137, 136, 135, 40, 43, 134 and 71, respectively (compounds 6 and 8 are not identified). Example 3 (pg 62-67) is titled "Activity of Polypeptides on Food Intake" and shows that administration of Compounds 1-127 reduces food take when administered intraperitoneally to mice (see the Table beginning on page 2). Compounds 1-127 are not identified in the original specification, but a preliminary amendment filed at the time of filing (8/10/06) amends the table to identify a number of the Compounds by SEQ ID NO. Compound 1 is identified as the elected species, SEQ ID NO: 137 and other compounds are identified as SEQ ID NO: 40-66 and 69-136. Example 4 (pg 67-68) is titled "Activity of Compounds of the Invention on Weight Reduction and Caloric Intake", and includes a table showing the

"percent body weight loss" at week 1 and 2 in rats receiving one of Compounds 1-9. Figures 2A and 2B provide the same results with more detail for Compounds 3-5 (SEQ ID NO: 135, 40 and 43). Example 5 (pg 68-69) is titled "Body Composition" and provides results (also shown in Figure 3), that "fat content was reduced in rats treated with Compound 1 compared to controls. Example 6 (pg 69-70) is titled "Gastric Emptying and Ion Calcium", and shows the dose response Compound 1 on rats in a Gastric Emptying Assay (Figure 4A) or on Hypocalcemic effect (Figure 4B). Example 7 (pg 70-72) is titled "Triglycerides" and reports that "[a]s indicated in Figures 5 to 7E, studies 1, 2 and 3, respectively, treatment with Compound 1 [SEQ ID NO: 137] over 1-8 weeks resulted in significantly lower triglyceride concentrations" (pg 71). Example 8 (pg 72-73) is titled "Ghrelin Assay" and "provides an exemplary assay for detecting the effect of the compounds of the invention on ghrelin". Example 9 (pg 73) is titled "Pancreatic Function", and shows that "treatment with Compound 1 [SEQ ID NO: 137] attenuated increases in pancreatic enzyme activities in the blood in rat model of acute pancreatitis" (Figures 9A and 9B). Examples 10-11 (pg 73-77) are directed to amylin rather than one of the peptides of the invention; Example 10 describes "Gastric Acid Secretion of Amylin" and Example 11 (pg 75-77) describes "Gastroprotective Effects of Amylin".

The elected species of peptide, SEQ ID NO: 137, is 32 amino acids in length. This peptide is a chimeric peptide comprising sequences derived from amylin and calcitonin. The loop and C-terminal regions (amino acids 1-7 and 28-32) are derived from either human or rat amylin (which share the same first seven and last five amino acids). The α helix region (amino acids 8-27) includes sequences derived from both amylin (human and/or rat) and salmon calcitonin. As described above, in Example 4 the specification provides evidence that a peptide of SEQ ID NO: 137 can reduce food intake when administered to mice. Thus, the specification enables the skilled artisan to make and use a peptide of SEQ ID NO: 137. Furthermore, Example 4 provides similar evidence for the peptides of SEQ ID NO: 40-66 and 69-136. Thus, the specification also enables the skilled artisan to make and use peptides of SEQ ID NO: 40-66 and 69-136.

Claims 12, 20, 22, 24, 26, 27 and 29 are each directed to a genus of peptides having a recited % identity to SEQ ID NO: 137; the broadest of these is claim 20, which recites a peptide having at least 87% identity. A variant of SEQ ID NO: 137 with at least 87% sequence identity can have up to 4 amino acid changes (28/32 = 87.5%). At least 80 of the peptides of SEQ ID NO: 40-136 fall within this genus. Others have more changes; e.g., SEQ ID NO: 126 has five substitution mutations with respect to SEQ ID NO: 137, resulting in 86.2% identity. However, the genus of peptides that are at least 87% identical to SEQ ID NO: 137 contains far more peptides than were tested in the instant specification. This genus is very large but is of a magnitude that can be made and screened by the skilled artisan to identify functional variants. Thus, in view of the results presented in the specification based on the administration of SEQ ID NO: 137 or variants thereof, the specification provides enablement for SEQ ID NO: 137 or a peptide having at least 87% sequence identity to the amino acid sequence of SEQ ID NO: 137, and wherein said peptide retains the functionality of SEQ ID NO: 137 (e.g., reduces food intake when administered to a mouse).

However, the specification fails to provide enablement for the following embodiments:

(1) The specification fails to provide enablement for a peptide having at least 87% sequence identity to the amino acid sequence of SEQ ID NO: 137, and that does not retain the functionality of SEQ ID NO: 137 (e.g., reducing food intake when administered to a mouse). The claimed genus of peptides having at least 87% identity to SEQ ID NO: 137 includes functional variants, but in view of the teachings of the art (cited below) would also be predicted to include many variants in which the amino acid changes result in a non-functional peptide. The specification does not teach how to use a peptide variant of SEQ ID NO: 137 that does not retain the functionality of SEQ ID NO: 137.

(2) While claims 12, 20, 22, 24, 26, 27 and 29 (and dependent claims 30 and 31) are limited to peptides that have at least 87% identity to SEQ ID NO: 137, claims 1-6, 8, 10, 18 and 19 are each directed to a broader genus of variant peptides. The broadest claim (claim 1) encompasses an amylin family peptide, said peptide comprising: a loop

region of amylin, calcitonin, or an analog of amylin or calcitonin, wherein said loop region is at the N-terminal end of said peptide; an α helix region of a) at least a portion of a calcitonin α helix region or an analog thereof or b) a combination of at least a portion of a calcitonin α helix region or an analog thereof and at least a portion of an amylin α helix region or an analog thereof; and a C-terminal tail of amylin, calcitonin, or an analog of amylin or calcitonin; with the proviso that when the loop region is from a calcitonin or a calcitonin analog and the α helix region is from a calcitonin or a calcitonin analog, the last position of the C-terminal tail is not proline, hydroxyproline, homoserine or derivative of homoserine. Such a genus is essentially limitless, because the amylin or calcitonin from which the sequence is derived is not limited to a particular sequence (and thus includes any mutated variant) and "a portion" can be as small as one amino acid in length.

Claims 2-5, 6, 8, 10 and 18-20 depend from claim 1 and are each directed to a subgenus of peptides. Even the narrowest of said subgenera (claim 10) encompasses a vast number of variants. The peptide of claim 10 encompasses at least 4.2×10^{11} different peptides based on the 20 standard amino acids ($4.2 \times 10^{11} = 6 * 3 * 3 * 3 * 2 * 1 * 2 * 2 * 2 * 3 * 3 * 1 * 5 * 7 * 6 * 1 * 3 * 5 * 3 * 2 * 2 * 5 * 1 * 2 * 1 * 1 * 2 * 1 * 1 * 4 * 2 * 3$). Each genus encompassed by the other claims is even larger.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry 29(37): 8509-8517; Ngo et al. (2 March 1995) "The Protein

Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research 10:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. 18(1): 34-39; Doerks et al. (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics 14(6): 248-250; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics 15(4): 132-133].

Due to the large quantity of experimentation necessary to generate the large number of variants recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 1-6, 8, 10, 12, 18-20, 22, 24, 26, 27 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicants are claiming and what Applicants have possession of.

The claims are genus claims for the reasons set forth above in the section titled "Claim Rejections - 35 U.S.C. 112, 1st paragraph, enablement". Claims 12, 20, 22, 24, 26, 27 and 29 (and dependent claims 30 and 31) are limited to peptides that have a recited % identity to SEQ ID NO: 137 (87% being the largest variation permitted), but do not limit the encompassed peptides to functional variants that retain the functionality of SEQ ID NO: 137. The specification fails to describe how to use a peptide variant of SEQ ID NO: 137 that does not retain the functionality of SEQ ID NO: 137. Claims 1-6, 8, 10, 18 and 19 are each directed to a broader genus of variant peptides. Each genus is highly variant because a significant number of structural differences between genus members are permitted.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide

sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus of claimed peptides. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the peptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed" (pg 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (pg 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of peptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an amylin family peptide having at least 87% sequence identity to the amino acid sequence of SEQ ID NO: 137, and wherein said peptide reduces food intake when administered to a mouse, but not the full breadth of the claim meets the

written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see pg 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Shigeaki et al (1996. Biochemistry and Molecular Biology International. 40(5): 923-929).

Claim 1 encompasses the following embodiment: a peptide comprising a loop region of calcitonin at the N-terminal end of the peptide, an α-helix region of at least a portion of a calcitonin α-helix region, and a C-terminal tail of calcitonin, with the proviso that when the loop region and the α helix region are from a calcitonin, the last position of the C-terminal tail is not proline, hydroxyproline, homoserine or a derivative of homoserine. The instant specification teaches that amino acids 1-7 of calcitonin are the loop region, amino acids 8-27 are the α helix region, and amino acids 27- or 28-32 are the C-terminal region. Thus, claim 1 encompasses a calcitonin peptide wherein the final residue (proline 32) is mutated, but where the rest of the protein is unchanged.

Shigeaki et al teach that "deletion of proline-amide from the C-terminus of human CT [calcitonin]". In the absence of this proline, the final amino acid of human calcitonin is alanine instead of proline (see amino acid sequences at pg 10 of the instant specification). Thus, Shigeaki et al teach a peptide comprising a loop region of calcitonin at the N-terminal end of the peptide, an alpha helix region of at least a portion of calcitonin, and a C-terminal tail of calcitonin, with the proviso that when the loop region and the α helix region is from a calcitonin, the last position of the C-terminal tail is not proline, hydroxyproline, homoserine or derivative of homoserine. Thus, the teachings of Shigeaki et al anticipate claim 1.

Claim 2 depends from claim 1 and recites "wherein said amylin is a human amylin or analog thereof". As set forth above in the section titled, "Claim Rejections - 35 U.S.C. 112, 2nd Paragraph", claim 2 is indefinite because it is unclear which recitations of "amylin" it limits in the parent claim, and has been interpreted as limiting one or more of the recitations of the parent claim. As such, claim 2 encompasses a peptide of claim 1 that is a "A human amylin family peptide, said peptide comprising...." Such a peptide includes those with the sequence as described above for claim. Thus, the teachings of Shigeaki et al also anticipate claim 2.

Claim 3 depends from claim 1 and recites "wherein said calcitonin is a salmon calcitonin". As set forth above in the section titled, "Claim Rejections - 35 U.S.C. 112, 2nd Paragraph", claim 3 is indefinite because it is unclear which recitations of "calcitonin" it limits in the parent claim, and has been interpreted as limiting one or more of the recitations of the parent claim. As such claim 3 encompasses a peptide of claim 1 that includes an alpha helix region of "at least a portion of a salmon calcitonin alpha helix region". While the teachings of Shigeaki et al are directed to human calcitonin, the human calcitonin α helix region includes "at least a portion of a salmon calcitonin alpha helix". Specifically, the alpha helix of human calcitonin includes the amino acid residues "LG", which are also found in salmon calcitonin. Thus, the human calcitonin peptide described by Shigeaki et al includes "at least a portion of a salmon calcitonin alpha helix". Thus, the teachings of Shigeaki et al also anticipate claim 3.

Claim 4 depends from claim 2 and recites "wherein said calcitonin is a salmon calcitonin". Thus, this claim combines the limitations of claims 2 and 3 above. Therefore, claim 4 is anticipated by the teachings of Shigeaki et al for the same reasons as for claims 2 and 3.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not

identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8, 10, 12-13, 18-20, 22, 24, 26, 27 and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,399,744 (filed 5/20/04; published 7/15/08). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

As indicated by Applicants in their response filed on 1/21/10, each of claims 1-6, 8, 10, 12-13, 18-20, 22, 24, 26, 27 and 29 read on the elected species of peptide, which is SEQ ID NO: 137.

Claim 1 of the '744 patent is directed to a method for reducing body fat or body fat gain in a subject, while maintaining or increasing lean body mass, comprising administering to the subject an amylin agonist comprising the structure of SEQ ID NO: 5; thereby, reducing body fat or body fat gain while maintaining or increasing lean body mass. Claims 2-7 depend from claim 1.

The following alignment, where Qy is instant SEQ ID NO: 137 and Db is SEQ ID NO: 5 of the '744 patent, shows that the two sequences are 100% identical:

```
  Query Match             100.0%;  Score 174;  DB 3;  Length 32;
  Best Local Similarity   100.0%;
  Matches   32;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 KCNTATCVLGRLSQELHRLQTYPRTNTGSNTY 32
              ||||||||||||||||||||||||||||||||
Db          1 KCNTATCVLGRLSQELHRLQTYPRTNTGSNTY 32
```

No restriction requirement was made in the '744 patent between the product and methods of use thereof. Therefore, the method of use of SEQ ID NO: 5 in the '744 patent anticipates the product claims in the instant application.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Bridget E Bunner/
Primary Examiner, Art Unit 1647